An Investigation of the Impact of Inflammatory Bowel Disease on the Psychosocial Functioning of Children and Teenagers in New Zealand

A thesis submitted in partial fulfilment of the requirements for the degree of Master of Arts in Child and Family Psychology at the University of Canterbury

by

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Abstract

Worldwide rates of Inflammatory Bowel Disease (IBD) have been dramatically rising in recent years and New Zealand has one of the highest rates of IBD in the world. IBD has the potential to affect many areas of functioning. Health-related quality of life is an outcome measure that attempts to take into account the lived experience of the individual, and is becoming increasingly more relevant to current research and understanding of the impacts of IBD on individual functioning. Research regarding this topic is limited at best, particularly among the paediatric IBD population. To date, only one study has been published that investigates that impact of IBD on the HRQoL of children and adolescents in New Zealand. The current study aims to further investigate the HRQoL of children and adolescents with IBD in New Zealand and to understand what factors might affect overall HRQoL.

It was hypothesised that (1) the IMPACT-III measure of HRQoL would exhibit good to excellent reliability scores, (2) duration of disease would predict HRQoL, (3) disease severity would predict HRQoL, (4) disease severity would significantly predict social functioning and (5) disease severity would predict scores on the other individual subscales of the IMPACT-III.

Results indicated that the IMPACT-III measure demonstrated good to excellent reliability scores, (2) duration of disease was not a predictor of HRQoL, (3) disease severity did predict HRQoL, and (3) disease severity predicted social functioning. These findings provide further evidence that disease severity is a significant influence on the HRQoL of paediatric individuals with IBD, highlighting the importance of treating these patients quickly and effectively to reduce the detrimental impact on HRQoL. Findings also suggest that assessment of HRQoL could be a beneficial component of routine assessment could be beneficial in identifying those individuals who are at greatest risk for poor developmental and HRQoL outcomes.

What is Inflammatory Bowel Disease?

Inflammatory Bowel Disease, commonly referred to as IBD, is a chronic autoimmune condition that causes ulceration and inflammation in the intestines (Kahui, Snively, & Ternent, 2017). According to current diagnostic practices, IBD includes a group of diseases known as Crohn's Disease (CD), Ulcerative Colitis (UC) and IBD unclassified (IBDU; (Day, Lemberg, & Gearry, 2014). Although these diseases fall under the single umbrella of IBD, CD and UC present differently, with inflammation from UC occurring in the inner lining (i.e., mucosal wall) of the large colon, while inflammation with CD can be found anywhere in the digestive tract (Banez & Cunningham, 2009). An IBDU diagnosis on the other hand, is assigned to those who have colitis but do not have the typical features that would enable a diagnosis of either CD or UC (Wilson & Russell, 2017).

Cause of IBD

While no aetiology for IBD has been clearly established (Denmark & Mayer, 2014), it has become widely accepted that an abnormal immune response in genetically predisposed individuals is triggered by a variety of environmental factors (Matsuoka & Kanai, 2015). Many experts concur that a genetic background plays a role in IBD, and more than 200 IBD susceptibility genes have been identified by genome-wide association studies thus far (Matsuoka & Kanai, 2015).

Genome-wide association studies have identified 28 overlapping susceptibility loci shared between CD and UC that are involved in host responses to gut microbiota. Analyses of these genetic loci highlighted the importance of the different pathways that are involved in gut homeostasis, regulation of innate and adaptive immunity, microbial defence, and autophagy

(Denmark & Mayer, 2014). For example, the first susceptibility gene identified for CD was NOD2, which is involved in inflammatory responses to bacterial triggers (Hampe et al., 2001). Therefore, it is no surprise that siblings of CD patients have an estimated lifetime risk of 5-10% of developing CD (Wilson & Russell, 2017), and concordance rate for monozygotic twins is around 20% for UC and 40-60% for CD. This suggests that CD might have more of a genetic basis than UC, however given that these rates account for less than 100%, it is likely there are other factors playing a role (Denmark & Mayer, 2014).

A key factor in the abnormal immune response associated with IBD is the microbiome within the gastrointestinal system. A healthy gastrointestinal tract involves a complex system of a large number of microbes that are essential to maintaining normal gut health. A prominent hypothesis in the cause of IBD relates to a reduction in the bacterial diversity and its loss of function, consequently leading to an increase in the number of pathogenic microbes within the gut (Wilson & Russell, 2017). Consequently, IBD patients appear to have strong immune responses to common bacterial antigens that don't trigger an immune response in a healthy host (Denmark & Mayer, 2014). These strong immune responses are thought to be triggered by exposure to environmental risk factors, which have been implicated in the onset of IBD.

A number of risk factors have been identified thus far, which include cigarette smoking, consumption of pro-inflammatory food, antibiotics, stress, air pollution, gastrointestinal infection, urban versus rural lifestyle, and vitamin D levels (Wilson & Russell, 2017). However, this is further complicated by the fact that the impact of some risk factors is known to differ between CD and UC. For example, cigarette smoking is a protective factor for UC, but a risk factor for CD (Wilson & Russell, 2017).

Prevalence of Inflammatory Bowel Disease

Worldwide.

A worldwide systematic review of the incidence and prevalence rates of IBD found that IBD was more common in western nations. Some of the highest incidence rates of CD and UC are found in the United States of America (USA), Canada, Southern Australia, New Zealand, the United Kingdom and Sweden. Temporal trends were investigated in this review, which indicated that 60% of the included studies had statistically significant increases in incidence rates of CD and UC, while only 6% indicated decreasing incidence rates. Overall this review indicates a significant increase in the occurrence of IBD as well as a predicted rapid rise in IBD's prevalence if current trajectories are maintained (Molodecky et al., 2012). The critical point to note from this review is that New Zealand is reported as being one of those countries with the highest prevalence and incidence rates in the world.

It is of concern that studies into the prevalence of IBD in the paediatric age group are somewhat limited. Of the available studies, one in Sweden found IBD prevalence rates were 75 per 100,000 (differentiated to 30 per 100,000 for UC, 29 per 100,000 for CD, 16 per 100,000 for patients with IBDU); (Ludvigsson et al., 2017). Similarly, a Canadian study in 2005 identified comparable prevalence rates for paediatric IBD of 56.3 per 100,000 (differentiated to 19.7 per 100,000 for UC and 23.9 per 100,000 for CD). When the authors compared these prevalence rates to data from 1994, it was found that these rates had increased significantly (Bernstein et al., 2006).

In 14 Northern California counties in the USA, the average annual standardised incidence per 100,000 was 2.7 for CD, 3.2 for UC, and 0.5 for IC/IBDU, which was an increase over the study period of nine years. The age-standardised point prevalence per 100,000 was 12.0 for CD, 19.5 for UC and 3.5 for IC/IBDU. These rates appear to be much lower than aforementioned

studies, however it is important to keep in mind the differing methodologies and classifications used in prevalence and incidence studies that might affect resulting prevalence and incidence rates (Abramson et al., 2010).

New Zealand.

Further to the worldwide studies that show significant prevalence rates that have been increasing over time for both adult and paediatric patients with IBD, New Zealand statistics demonstrate extremely high rates of IBD, which are comparative to those worldwide. While only a few epidemiological studies have been conducted in New Zealand, a study dating back to the 1980's showed very low rates of both CD and UC in adults, which are in stark contrast to more recent studies (Eason, Lee, & Tasman-Jones, 1982; Schulp, Maclaurin, Barbezat, & Lambert, 1986). In 2004, the point-prevalence of IBD in Canterbury, New Zealand was 308.2 per 100,000 people (i.e., 155.2 for CD, 145.0 for UC, 8.0 for IC/IBDU; Gearry et al., 2006). The incidence rate of IBD was 25.2 per 100,000 (i.e.,16.5 for CD, 7.6 for UC, and 1.1 for IC/IBDU), with a peak incidence between 20 and 34 years of age. In the study cohort, more females had CD than males, however, the gender difference was smaller for UC.

A follow-up study conducted in 2014 found that 205 people were diagnosed with IBD in one year alone (Su, Gupta, Day, & Gearry, 2016). The crude incidence rates of IBD had increased to 29.8 per 100,000 (i.e., 26.0 for CD, 13.4 for UC, and 0.39 for IBDU). The age-standardised rate, which accounts for the differences in the age structure of populations, was one of the highest in the world for CD. The gender of cases in this study was evenly distributed with almost half of patients being male. Similar to the earlier Canterbury study, more females had CD, but this was not a statistically significant difference.

Paediatric IBD in New Zealand.

The first paediatric study of IBD incidence in New Zealand found rates lower than those in North American and European countries. Incidence rates of new cases of paediatric IBD from 2002-2003 were estimated at 2.9 per 100,000 per year. However, it is important to note that this study only included those aged younger than 15, and relied on elective reporting by paediatricians and specialists, who were contacted monthly. They reported that there were no Māori or Pacific Islanders with CD, and regionally prevalence was highest in the South Island (Yap, Wesley, Mouat, & Chin, 2008).

In a more recent study, Lopez et al. (2017) examined the nationwide prevalence of IBD in New Zealand, finding that there were 212 children under the age of 16 living with IBD, with a point prevalence of 21.7 per 100,000 children. Further examination indicated prevalence rates of 16.5/100,000 for CD, 3.3/100,000 for UC, and 1.9/100,000 for IBDU. Although IBD was prevalent in every region across NZ, rates were found to be much higher in the South Island, with an estimate of 60 children per 100,000 having a diagnosis of IBD, compared to 10 to 20 children per 100,000 in the North Island. Prevalence rates in this study were calculated from two databases, as well as a list of every patient seen and treated in Christchurch Hospital. Patients from the North Island were identified via the paediatric gastroenterologists from Starship Hospital, who prepared a list of every patient known to their service. This study also identified low rates of IBD in the indigenous populations in New Zealand, with diagnosis seen mostly in children and adolescents of European ancestry.

Symptom Presentation

IBD is an extremely unpredictable disease, with a course that often fluctuates between periods of active disease and remission. This, of course, is extremely idiosyncratic, where IBD is

known to affect each individual differently (Kahui et al., 2017). IBD manifests itself during childhood and adolescence in approximately 25% of patients (Griffiths, 2004), and presenting symptoms often differ as a consequence of the location and severity of inflammation in the digestive tract (Proctor & Kranzler, 1998).

The classic presentation of CD symptoms across all age groups includes diarrhoea, constipation, abdominal pain, poor appetite, and weight loss, with this presentation found in nearly 80% of children and adolescents who are diagnosed with CD. Although symptoms such as pauciarticular arthritis, short stature, and predominant perianal disease occur more rarely, bloody diarrhoea occurs in the vast majority of patients with UC and can be seen as a primary symptom (A. M. Griffiths, 2004). Many patients also experience many or some of the following symptoms; rectal bleeding, rectal urgency, fatigue, and fever. Children with IBD are more likely than adults to present with more extensive disease, and are more likely to have their upper gastrointestinal tract affected, as well as longer segments of inflammation in the small bowel (Lemberg & Day, 2015).

Less common symptoms of IBD such as poor growth, oral manifestations, anaemia, and perianal symptoms without any obvious abdominal pain or diarrhoea, often contribute to a delayed diagnosis, particularly in younger children (Lemberg & Day, 2015). It is also noted that the effects of poor nutrition can occur for years before intestinal symptoms start to manifest themselves. IBD patients are at risk of growth failure, delayed puberty and its potential medical issues, and permanent growth impairment. (Kelsen & Baldassano, 2008). Growth impairment typically occurs in around 30% of children with CD, and 5-10% with UC and is caused by multiple contributory factors that limit both overall nutrition and caloric intake. These include pain associated with eating, anorexia or inability to eat a full meal (Mallon & Suskind, 2010).

Children with IBD will typically grow slowly before diagnosis and during times of active disease, with low nutrition being cited as an important factor in this type of growth impairment (Turkel & Pao, 2007). The impact on the expected growth trajectory can be directly affected by the patients themselves as they may self-restrict their food intake due to the anticipated abdominal pain, cramps and diarrhoea that frequently accompany eating. (Proctor & Kranzler, 1998). This is particularly concerning considering that delayed puberty can contribute to a host of medical issues.

CD can contribute to reduced mineral bone density, partly as a result of impairments in muscle strength (Ward et al., 2017). It is not uncommon for delayed puberty to result in osteoporosis as there is typically a significant peak in mineral accumulation following the pubertal growth spurt. Furthermore, delayed puberty can affect estrogen and androgen production, which are important for bone mineralisation which occurs during this critical period, and subsequently contributing to bone mineralisation issues demonstrated in patients with CD (Kelsen & Baldassano, 2008).

Treatment and Treatment Goals

Unfortunately, IBD is a lifelong, chronic condition, and there is no cure. Currently, treatment is provided with the aim of controlling inflammation and inducing and sustaining periods of remission, while avoiding disease and drug-related complications and unnecessary surgery (Wilson & Russell, 2017). A particular patient's treatment regimen is based on the location and severity of the disease and may include 5-aminosalicylic agents, antibiotic therapy, corticosteroids, immunomodulators and biologic agents (Diefenbach & Breuer, 2006). The traditional 'step up' method is applied in most cases, and involves the use of less toxic, milder

medications first. Patients then move through more aggressive agents, as they are deemed to 'fail' a particular treatment method (Dubinsky, 2007).

Aminosalicylates are effective first-stage treatments for inducing and maintaining remission in patients with mild to moderate UC, however, evidence for its use in the treatment of active CD is less promising than for UC (Denmark & Mayer, 2014).

Corticosteroids are perhaps considered the most common treatment approach for autoimmune issues and are frequently used in the treatment of IBD, with many patients responding positively to an oral treatment course (Denmark & Mayer, 2014). However, many patients will experience unpleasant side effects, some of which include; mood, behavioural and sleep disturbance, osteoporosis, growth suppression, striae (i.e., stretch marks), acne, hirsutism (i.e., unwanted hair growth) and a Cushingoid appearance (i.e., facial swelling and weight gain ;King, 2003). These aesthetic side effects can be particularly upsetting for a child or adolescent (Dubinsky, 2007). For example, a qualitative study investigating the concerns of paediatric patients with IBD found that a primary concern was altered body image, which was devastating for some patients (Casati, Toner, Rooy, Drossman, & Maunder, 2000). Whilst many patients respond to a course of steroids, many will relapse once the dose is reduced or stopped, thus become dependent on corticosteroids to control their disease (T. Orchard, R. D. Goldin, P. P. Tekkis, & H. T. Williams, 2011).

When considering programmes for paediatric IBD patients it is vital to prevent, or if necessary, reduce the occurrence of poor growth. Consequently, corticosteroid medications are no longer used as widely or for long periods of time, as the impact on growth and physical development are well known. As growth only occurs until the end of puberty, aggressive treatment is often required to avoid poor growth. Although treating the disease itself can restore

typical growth, the often-utilized use of glucocorticoids in IBD patients, can also lead to growth impairment. Consequently, this can result in a higher incidence of side effects such as osteoporosis, cataracts, and glaucoma in younger patients when compared to adult patients (Turkel & Pao, 2007).

As an alternative to corticosteroids, exclusive enteral nutrition (EEN) is now the standard approach to induce remission in children with CD. One advantage of this treatment is the ability to correct nutritional deficits, as well as induce mucosal healing (Schultz et al., 2010). EEN involves the use of liquid formula as 100% of caloric needs and has been shown to be particularly effective at inducing clinical remission in children with IBD (Rosen et al., 2015). High-calorie supplements can be effective in improving growth by raising a patient's daily caloric intake, which can prevent the disruption of the normal growth curve over time (Proctor & Kranzler, 1998).

While EEN therapy usually only lasts approximately 6-12 weeks, it requires the patient to follow a strict liquid formula diet and is often used in combination with maintenance medical therapy (Rosen et al., 2015). In more severe cases, nasogastric feeding tubes are required particularly for those who cannot tolerate oral ingestion of supplements, which contributes to the fact that this form of nutrition is typically not well-liked by patients (Proctor & Kranzler, 1998). This treatment method has demonstrated that it can be as effective as an oral steroid at inducing remission without the side effects that come alongside steroid treatment (T. Orchard, R. Goldin, P. Tekkis, & H. Williams, 2011).

Thiopurines are a class of immunosuppressant drugs that are often used in order to allow for the discontinuation of steroids where frequent use is required, with their effectiveness confirmed in clinical studies. Although side effects are less common than for steroids, patients

can experience leukopenia, pancreatitis and potentially hepatitis (Mackay & Rose, 2013). Methotrexate, another type of immunosuppressant, is often used as an alternative to thiopurines (Lemberg & Day, 2015). Corticosteroids, 5-aminosalicylates and immunosuppressants have long comprised the standard tools for the treatment of IBD patients (Vogelaar, Spijker, & Woude, 2009), however they often fail to prevent disease progression and induce long term remission (Xu et al., 2014).

Anti-TNF biologic medications are known to avoid growth failure in adolescents and can be considered first-line treatment for growth delayed children and adolescents with CD, particularly those who are near the end of puberty (Crohn's and Colitis Canada, 2018). Acquiring these medications can be troublesome however, as the traditional approach often requires children to fail on therapies such as corticosteroids, immunotherapies and surgery before such medications can be considered (Schultz et al., 2010). In New Zealand, biologics are indicated in moderate to severe pediatric CD, but are not currently funded for UC. The utilisation of the biologic medications in New Zealand are controlled via a special authority process administered by PHARMAC, the government agency responsible for decisions regarding the funding of medications and access or specific disease classes (Schultz et al., 2010)

Whilst also addressing the issues associated with growth, the newer biologic drugs such as Infliximab (IFX), are shown to be effective in inducing and maintaining long-term remission in IBD patients, particularly those for which traditional treatments have been ineffective (Denmark & Mayer, 2014). While biologics appear to be more effective in inducing remission, they are much more costly than traditional treatments and access is restricted. Their cost effectiveness is in their ability to rapidly induce long term remission which is known to be associated with a lessened need for medical care and better quality of life overall for the patient.

(Vogelarr et al., 2009)

'Top-down' methods, or the earlier introduction of biologic therapies are becoming increasingly adopted, particularly in those patients who are found to fail the early conventional treatments (Crohn's and Colitis Canada, 2018). This approach is not ideal for all patients, particularly those who are able to be managed with traditional treatments that are known to have a lower risk of systemic toxicity (Hirschmann & Neurath, 2017).

Sometimes instead of, or in addition to medical management, surgery is required to induce remission or to treat disease-related complications (Lemberg & Day, 2015). As with pharmacological treatment, surgery does not cure the disease, and recurrence occurs within 5 years, on average (Proctor & Kranzler, 1998). Surgery often involves the removal of diseased bowel, which sometimes requires the creation of an intestinal ostomy (Rosen, Dhawan, & Saeed, 2015) which is an artificial surgically created opening in the skin (stoma). This allows for waste to exit the body, bypassing parts of the large or small bowel, and can be a permanent or temporary measure (Borkowski, 1998).

The Impact of Inflammatory Bowel Disease

Financial cost.

Few studies have documented the financial cost of IBD in New Zealand, but it is becoming increasingly relevant given the increased use of newer, more expensive therapies, and the increasing prevalence of the disease. In their study, Lion, Gearry, Day, and Eglinton (2012), evaluated the direct and indirect costs of CD in paediatric and perianal patients in Canterbury, New Zealand. They found that on average, the total cost in 2012 per patient for paediatric CD was $14,375, comprising $12,583 for direct costs (classified as hospital and outpatient costs),

and $1792 for indirect costs (classified as lost productivity, travel, carers, tutors and additional phone for internet requirements). Of the identified costs, outpatient costs were found to be the most significant direct cost, followed by pharmaceutical costs, whereas absenteeism from work was identified as the most significant indirect cost. From these indirect and direct costs, it was estimated that the total cost of paediatric and perianal CD in one year was between $25.9 and $36.7 million, thus confirming that these diseases are high-cost disorders (Lion et al., 2012). In 2016, Pharmac funded medications cost New Zealanders around $29 million NZD, which is staggering when one considers that this figure only includes identifiable costs for IBD (Kahui et al., 2017).

As a comparison to costs in New Zealand, a review of newly diagnosed IBD patients in Australia found that CD was the most expensive, with average costs per patient of $10,477, followed by $6292 per patient for UC. The increased costs for CD were as a result of the higher use of diagnostic tests and specialist visits (Niewiadomski et al., 2015). The cost figures did not include indirect cost assessments, which may account for the slightly lower per-patient costs than the aforementioned study assessing costs in New Zealand. Similarly, Bassi, Dodd, Williamson, and Bodger (2004) investigated the cost of IBD in the United Kingdom, estimating average total costs for six months at £757,433, which can be broken down to an average cost of £1652 per CD patient, and £1256 per UC patient. Comparatively, a Canadian review of the burden of IBD, estimated direct medical costs for treating IBD, noting that patients with IBD often need medical care despite when their disease is in remission (Rocchi et al., 2012). This review estimated that in 2012, total direct medical costs were over $1.2 billion, with drug costs, followed by inpatient hospitalisation consisting of 76% of the total direct medical costs of IBD. Indirect costs were estimated at over $1.6 billion, and other costs (i.e., laboratory tests and procedures, non-

physician professional services, home-care and long-term care) were estimated at $101 million. For paediatric patients with IBD, at least one parent was required to be involved in the care of that child, and had to take time off work to provide care when the child was not well enough to attend school, which could result in short-term or long-term work losses depending on the severity of their child's disease.

While it is difficult to make clear comparisons of costs between countries, the cost per patient in New Zealand appears to be similar, if not more costly compared to other countries (Bassi et al., 2004; Lion et al., 2012; Niewiadomski et al., 2015). Differing methodologies and cost calculations should be considered when comparing the above studies, however, it is noted that the cost of IBD in New Zealand is significant.

Physical functioning.

Given the host of IBD related symptoms that young people with IBD often suffer, it comes as no surprise that their physical functioning may be impaired. Physical functioning is also closely linked to other areas of functioning, including social functioning, emotional functioning, education and learning, and body image and self-esteem. For example, to assess physical functioning as part of an overall health-related quality of life assessment, the IMPACT-III questionnaire includes questions about energy levels, how tired the individual has felt, and how they have felt in the past few weeks (Otley et al., 2006). Similarly, the generic HRQoL measure, the PedsQL Generic Scale (4.0) contains questions about energy levels, amount of pain, and ability to participate in sport and other physical activities (Varni, Seid, & Kurtin, 2001). A study by Pinquart and Teubert (2012) completed a meta-analysis to integrate results of 954 studies that discussed levels of physical, social, and academic functioning to healthy peers. The

findings from this analysis demonstrated that those with chronic illness had significantly lower physical, academic, and social functioning compared to their healthy peers. When comparing those in the sample with IBD to healthy peers, moderate effect sizes were exhibited.

One particular aspect of physical functioning that may be considered as a measure is the participation in physical activity. It is known that individuals with chronic disorders are less physically active than their healthy counterparts. Currently there is limited data assessing physical activity in paediatric patients with IBD, however, one study by Werkstetter et al. (2012) showed a reduced duration of high-level activity, number of steps, and increased sleep duration in 39 paediatric IBD patients when compared to healthy controls. Further, the study reported that disease severity was a significant correlating factor where participants with mild disease were sleeping 30 minutes longer, and completing half an hour less physical activity per day, when compared to those with inactive disease. This study also emphasises the potentially detrimental effects IBD can have on physical activity, particularly given that participants included were those with disease in remission or those with mild disease. Thus, it is easy to propose that the levels of activity may be reduced even further in patients with moderate to severe disease activity. Another study found disease activity has been associated with greater impairment in sports participation in adolescents with IBD (Plevinsky, Wojtowicz, Poulopoulos, Schneider, & Greenley, 2018).

Fatigue, which is a common complaint among patients with chronic illness is yet another example of the physical impact of IBD on children and adolescents (Marcus et al., 2009). Fatigue is considered to be an overwhelming feeling of tiredness or weakness, that is typically unrelieved by sleep or rest and can reduce both the ability and motivation to participate in physical activities. This can have a negative effect on social interaction, as opportunities and exposure to others in social situations may be reduced thus contributing to social isolation (Czuber-Dochan,

Ream, & Norton, 2013). While few studies have examined the prevalence of fatigue in the paediatric IBD population, a review of research investigating IBD-fatigue in adults found reported rates of 22-36% for UC and 27-41% for CD. These rates are staggering when one considers that these rates were for patients who were deemed to be in 'remission', however patients with active CD reported fatigue rates of 72-77% (Czuber-Dochan et al., 2013). A further finding of this study noted that paediatric patients with IBD reported fatigue scores comparable to children with cancer and rheumatologic diseases.

Body image and self-esteem.

Self-esteem considers an individual's attitude about themselves and is an important factor in quality of life. Development begins from infancy, continuing throughout life (Lindfred, Saalman, Nilsson, & Reichenberg, 2008), and it is during childhood that the ability to successfully learn new skills and accomplish challenging tasks, interacting with peers and succeeding at school are critical activities in the development of self-esteem. For children with a chronic illness, this process can be hampered by the lack of ability to participate in sports or activities with peers, particularly if they have extended periods in hospital. As adolescence is often characterised by a period of desire for more independence and peer approval, chronic illness has the potential to interfere with these ideas due to treatment requirements, physical changes, and limits set by parents, which are often due to recommended medical guidelines (Vitulano, 2003).

Many children and adolescents require surgery sometime during their treatment programme to manage their disease. In some cases, as described previously, a stoma may be required to divert faecal matter outside the body. This surgery often results in significant body

changes that must be adapted to, and requires an adjustment to daily care routines. As has been discussed before, adolescence is a particularly critical period of development, where these issues of acceptance and body image issues can be further highlighted (Diefenbach & Breuer, 2006).

An ethnographic study, which incorporated qualitative interviews and focus groups, identified common experiences of adolescents with IBD and ostomies (Griffiths et al., 1999). One of the key themes identified was body intrusion and body image changes. While self-consciousness about body image changes, and concerns regarding the appearance of their stoma was prevalent, participants also discussed increasingly adjusting to the appearance of their stoma over time. Another concern discussed was self-consciousness and worry that others would notice their stoma and ask them questions about it (Griffiths et al., 1999).

Research has been conducted that examines the perceptions and beliefs of young people with IBD regarding themselves and their disease. In a qualitative examination of challenges that children and adolescents with IBD face, a common theme that emerged was one of how participants viewed their lives as being different from others. Specifically, individuals with IBD indicated frequent physical comparisons to their peers, as well as difficulty engaging in activities that others deem typical. Additionally, some participants described not being able to go out socially when they are sick, feelings of wanting to look thinner to peers, or how going out would be a waste of time if they didn't feel good. Appearance-related teasing by peers was also described, such as being mocked about their appearance. Finally, male participants described frustration with not being as tall, fast or strong as their peers, and missing out on activities due to a lack of energy, which they felt left them with fewer friends (Nicholas et al., 2007).

Similarly, research focusing-on self-esteem among children and adolescents with IBD presents mixed findings. For example, in a study conducted by Engstrom (1992), self-esteem

levels were compared for children with IBD, chronic tension headaches, diabetes, and healthy children with no chronic physical disease. The children with IBD and headaches scored significantly lower than the healthy children group on their self-esteem, and the diabetes group only scored slightly lower than the healthy children group. In a similar study, children with IBD and children with paediatric headache scored lower on measures of self-esteem than their healthy counterparts (Engstrom, 1999). Conversely, Mackner and Wallace (2005) found that there were no significant differences between the children with IBD and healthy children on their measures of self-esteem, and mean scores recorded were within the expected normal range. Similarly, Lindfred et al. (2008), reported that self-esteem in adolescents aged 10-16 years with IBD was comparable to that of healthy references. However, disease severity was found to be a predictor of self-esteem, where participants with severe disease report lower self-esteem than those with mild disease.

Emotional functioning.

Given the multitude of disease-related challenges and symptoms that come along with IBD, children and young people with IBD are at risk for a number of psychosocial difficulties (Reed-Knight et al., 2014), particularly when disease onset often occurs in adolescence, which is a peak time for cognitive, social and emotional growth and change (Mackner et al., 2013).

A handful of studies have measured and described the negative impact of IBD on the emotional functioning in children and adolescents, namely, the occurrence of internalising symptoms or disorders. Few studies exist that have examined behavioural and emotional symptoms in paediatric IBD which have incorporated healthy comparison groups. Without these groups, it is impossible to determine if children and adolescents with IBD suffer from these

symptoms more than the general healthy population. For example, (Mackner & Crandall, 2006) reviewed the psychosocial functioning of adolescents who had a diagnosis of IBD for at least one year via administration of the Child Behaviour Checklist (CBCL), a widely used measure to assess emotional and behavioural problems in children and adolescents. Almost one-third of participants who had IBD reported clinically significant internalising symptom scores and total CBCL scores, however, this was not significantly different from healthy adolescents. Further, adolescents with IBD were reported to have more anxious or depressed symptoms, however mean scores were in the normal range. Similarly, no significant differences were found in any measures of behavioural or emotional functioning between those with IBD and healthy participants, with mean scores falling within the normal (non-clinical range). Although 20% of those with IBD demonstrated clinically significant total scores, these did not differ significantly from healthy adolescents. Interestingly, significantly more adolescents in the healthy group had externalising scores in the clinically significant range when compared to children with IBD in remission (Mackner & Crandall, 2006).

In a contrasting study, Engstrom (1992) found that 60% of children with IBD in a sample of 20 fulfilled the criteria for a psychiatric disorder based on the Child Assessment Schedule, which could yield a diagnosis according to the DSM-III-R classification. Diagnoses of those in the IBD group clustered around depressive and anxiety disorders. On this note, participants with IBD demonstrated significantly higher scores of depression, when compared to healthy controls, measured by the Children's Depression Inventory (Kovacs, 1981). Similarly, Szigethy et al. (2004), conducted a study with older children and adolescents with IBD and found that approximately 25% of youth in the study had depressive symptom scores that fell in the clinically significant range, measured by the Children's Depression Inventory (CDI). Pearson

correlations indicated that being diagnosed with IBD at a later age was associated with greater depressive symptomatology, however severity of disease was not associated with depressive symptom severity.

Social functioning.

An important aspect of quality of life is social functioning, and definitions of this construct typically encompass peer relations, social competence and social adjustment. This might include ideas such as; how individuals make friends, get along with others, participate in social groups, and navigate school and extracurricular activities (Adams, Streisand, Zawacki, & Joseph, 2002). Social functioning has been highlighted as a valuable indicator of behavioural and emotional problems in children, with changes in social functioning indicating difficulties with illness adjustment, problems with medical non-compliance, or general disease mismanagement. (Adams et al., 2002).

In patients with IBD, given the symptoms and potential severity of the illness, it is not difficult to imagine the potential for negative effects on the social functioning of a child or teen. The host of potentially unpleasant physical symptoms, such as diarrhoea, frequent bathroom visits, bowel urgency, and abdominal pain can lead to limitation of social activities to somewhere that predictable bathroom access is available. In some cases, young people may suddenly need to cancel planned activities entirely when they feel unwell and a young person experiencing a severe "flare up" of the disease, which might prevent them from participating in any social activities at all (Greenley et al., 2010). In one survey of children and adolescents with CD, 40% expressed concerns with the ability to stay overnight at friends' houses, and 50% thought they were unable to play outside with their friends (Moody et al., 1999). These difficulties hinder a

young person's development and maintenance of quality peer relationships, and can result in exclusion which further reduces opportunities for peer engagement and support (Suris et al., 2004). This can be particularly alarming given the move during adolescence to rely more on peers, rather than their parents for support (Vitulano, 2003).

It is clear that IBD has the potential to negatively affect social functioning in young people, however, literature with a focus on these social issues is limited at best, and those studies that do discuss social functioning appear to have mixed results (Boer, Grootenhuis, Derkx, & Last, 2005).

For example, in a study conducted by Boer et al., (2005) each subdomain of HRQoL was impaired among a sample of children with IBD, with the exception of the social functioning subdomain. Similarly, Varni et al. (2015) reported no differences in social functioning of those with IBD, when compared to healthy peers. Conversely, Abdovic et al. (2013), found that children who had more severe IBD had poorer HRQoL social functioning scores than those with less severe disease. These findings were consistent with previous findings that social functioning scores were poorer in those with more active disease (Chouliaras et al., 2017). In the same study, social functioning was positively related to disease duration and age, indicating that those who had the disease for longer or were older, had higher social functioning scores. Similarly, Hill et al. (2010) studied social functioning in young people with CD and found moderate negative correlations between disease severity and social functioning. Kunz, Hommel, and Greenley (2010) found that IBD patients had significantly higher social functioning when compared to a chronic illness group, but social functioning was still lower than that of healthy peers.

Education and learning.

A Crohn's and Colitis New Zealand Study (2017), found that carers for school-age dependants reported their children with IBD were missing 20 or more school days in the school year on average, in addition to missing other activities (e.g., school trips, sports, after-school extracurricular activities). Significantly, 77% of these carers also reported that IBD had more than a minimal effect on their dependant's education, with 26% reporting this as a major impact (Kahui et al., 2017). This is of significance, as education plays a major part in a young person's development, not only academically, but their overall quality of life (Suris, Michaud, & Viner, 2004). Further complicating this is New Zealand's dispersed rural population, who often have to travel a considerable distance to attend general practitioner and specialist appointments (Brabyn & Barnett, 2004), thus requiring more time off school to attend these appointments.

Mackner, Bickmeier, and Crandall (2012) completed a study that assessed the school functioning of youth with an IBD diagnosis. They found that adolescents with IBD had significantly more full-day absences from school than healthy adolescents, with 20% of the IBD group missing more than three weeks of school, compared to only 4% of the healthy adolescents. Grade Point Averages and school quality of life were also lower than that of the healthy youth, but these findings were not significant. Moody, Eaden, and Mayberry (1999), investigated the perceived impact of CD on school and family life by administering a questionnaire to 99 children aged 5-17 years with CD. Long absences from school were reported in 60% of participants, with an average of 3 months absence in the past 12 months. Those who had participated in exams believed they had suffered from underachievement as a result of their poor health. Additionally, Ferguson, Sedgwick, and Drummond (1994), administered a structured clinical interview to 70 young adults with paediatric onset IBD. They found that 40 reported two months or more

absence from school, typically at the time of onset of their disease, or for hospital admissions.

School is a core source of friendships for young people, and provides an environment where young people are able to spend extended periods of time to develop and grow their friendships (Vitulano, 2003). It is known that young people with IBD often miss a significant amount of school days each year (Ferguson et al., 1994; Kahui et al., 2017; Laura Mackner et al., 2012), resulting in limited opportunities to interact with peers leaving young people feeling that they are not involved and up to date with the relevant information in their social group (Vitulano, 2003).

Quality of Life

Traditionally, outcome measures of morbidity and/or mortality have been the focus of health outcome measurements, which may have included consideration of days hospitalised, number of infections, presence of side effects, and physician-rated objective clinical efficacy. However, little or no attention is paid to the patient and measuring the direct impact the disease has on their psychosocial well-being (Grant & Otley, 2017).

The utilisation of quality of life outcome measures has become more prevalent in recent years (Grant & Otley, 2017) along with the inclusion of patient-related outcomes (PRO's) that extend beyond the traditional health outcome measures. These measures include health data that is reported by the patient such as symptoms, satisfaction with therapy, treatment adherence and functional status (Marquis, Arnould, Acquadro, & Roberts, 2006).

Health-related quality of life (HRQoL) is one type of patient-reported data that can be used to measure the impact of chronic disease in individuals (Guyatt, Feeny, & Patrick, 1993). HRQoL is a multidimensional construct incorporating different domains of functioning,

including physical (e.g. energy levels, mobility), psychological/emotional (e.g. presence of anxiety, well-being, embarrassment about symptoms), academic (e.g. ability to attend school, effect on academic achievement), and social functioning (e.g. ability to make friends, openness about disease with others) (Office Of Disease Prevention and Health Promotion, 2010).

HRQoL focuses on quality of life as a consequence of the individual's health status and is often used to measure the effects of a chronic illness, treatments, or disability on the individual (Office Of Disease Prevention and Health Promotion, 2010). While the traditional clinical indicators of health status provide vital information to describe an individual's state of health, consideration of objective, patient-rated factors are essential to provide an overall assessment of HRQoL. Typical assessment of disease severity in an IBD patient relies heavily on the physician's perception of disease and the degree of intestinal inflammation (Marquis et al., 2006). Physiological indicators such as these are often less valuable or helpful for patients, and can be of greater interest to the clinicians. Further, these measures often correlate poorly with wellbeing and functional capacity (Guyatt et al., 1993). On the other hand, the HRQoL measures clearly shift the focus from the perspective of the clinician to that of the patient, and are designed to assess the impact of disease on the individual more comprehensively (Grant & Otley, 2017).

Quality of life and paediatrics.

Measurement of HRQoL in the paediatric population can be more problematic than doing so in an adult population, however it provides a valuable insight into the child's perception of their disease, particularly in the self-report measures. Parent-proxy measures of HRQoL have been shown to have poor agreement with self-reports in many cases, which highlights the need for the development and use of reliable, valid self-report instruments which take into account the

developmental level and age of the child. Incorporation of a HRQoL measure into clinical practice may be helpful in identifying physical and psychosocial health concerns that are often overlooked in paediatric patients (Varni, Burwinkle, & Lane, 2005), thus providing a mechanism to establish more reliable data to identify the psychosocial costs associated with IBD.

It is noted that there is often an under-identification of psychosocial problems in paediatric practice. The utilisation of HRQoL can address this issue, whilst also aiding physicians in identifying patients with physical and psychosocial health concerns, that could be addressed through treatment modifications, or referral onto other services (Varni et al., 2005).

Having effective strategies to measure HRQoL in paediatrics becomes more vital when one considers that young children may not have the communication skills to express their health-related concerns and feelings verbally. In these cases, parents often have to become the child's advocate, communicating to the physician on behalf of their child. HRQoL measures that are sensitive to such issues may be beneficial in a clinical setting and indicate problem areas that need attention from the perspective of the child (Varni et al., 2005).

Generic versus specific HRQoL.

In terms of assessing HRQoL, measures can be either generic or specific, with generic measures containing broad health-related questions, that are not specific to a particular disease. The use of generic measures allows clinicians and researchers to make comparisons of HRQoL across illness groups and to compare specific illness groups to healthy norms. A number of generic measures of HRQoL currently exist for use in the paediatric population (Solans et al., 2008): these vary in their structure and length, from assessments using single indicators, to multiple item measures that assess several dimensions of health (Grant & Otley, 2017). For

example, the Child Health Questionnaire (CHQ), measures HRQoL in children and adolescents aged 5-8 years and consists of a child report as well as two versions of a parent-proxy report. The child-report questionnaire contains 87 items, and has 4-6 response options. This measure assesses HRQoL across several domains including physical functioning, emotional, behavioural and physical functioning, bodily pain, general behaviour, mental health, self-esteem, general health perceptions, change in health family activities and family cohesion (Raat, Mangunkusumo, Landgraf, Kloek, & Brug, 2007).

On the other hand, while specific measures often cover similar issues to generic HRQoL measures, they address questions specific to the particular disease being assessed (Grant & Otley, 2017). By only containing HRQoL questions that are relevant to the disease in question, they are more responsive to changes in HRQoL as a function of changing disease characteristics. HRQoL measures can be specific to a particular disease (e.g., IBD, Asthma, Diabetes), population (e.g., elderly, children, pre-schoolers), function (e.g., mobility, sleep), or problem (e.g., pain). One advantage of using specific measures is that they often relate to areas that are assessed by clinicians. For example, disease-specific measures are becoming increasingly utilised as a secondary outcome measure in clinical trials of new pharmacological treatments (Guyatt et al., 1993).

Measurement of HRQoL in the adult IBD population has been the subject of a significant amount of research in recent decades. As a result, there now are validated outcome measures that are being utilised as an outcome measure in many clinical trials and research. For example, the Inflammatory Bowel Disease Questionnaire (IBDQ) is a 32-item questionnaire that covers four domains, including bowel symptoms, systemic symptoms, emotional functioning, and social functioning (Grant & Otley, 2017). Unfortunately, the development of disease-specific measures

for the paediatric population has lagged behind those for the adult population. In response to this, the IMPACT questionnaire was developed in the mid-1990s. REF HERE This is a self-report questionnaire is designed for the paediatric population, which is now available in over 40 languages.

HRQoL Paediatric Literature.

A literature search using Google Scholar, PsycINFO and the University of Canterbury's MultiSearch function was carried out to identify published studies that present findings on the HRQoL of children and adolescents with IBD. While many studies have been published regarding the HRQoL of adult patients with IBD, less attention has been paid to the paediatric population with IBD. Some studies have utilised generic HRQoL measures, while others have used measures designed for those with paediatric IBD. This would suggest that there is scope to further research validated and reliable measures and utilise tools that are specific to the paediatric population, and particularly those with IBD.

HRQoL comparisons with healthy peers.

Growing evidence examining the impact IBD can have on children and adolescents is being published with comparisons being made between young people with IBD and healthy peers. Intuitively, young people with IBD would have impaired overall HRQoL, and the research supports this hypothesis. Specifically, a study with 55 families of IBD patients aged 10-18 years completed the Child Health Questionnaire (CHQ), a generic HRQoL measure (Landgraf & Abetz, 1998). This measure is a 50-item scale that utilises both parent and child report and assesses 14 health domains. Disease severity of participants was assessed using the Harvey

Bradshaw Simple Index (HSBSI) which examines general wellbeing, abdominal pain, number of liquid stools per day, abdominal mass, and extra-intestinal manifestations. The study found that participants with IBD had significantly lower scores of physical and psychological health than their healthy peers. Further analyses showed that there were also significant group differences in 9 of the 12 dimensions on the CHQ (physical functioning, emotional/behaviour, physical role impact, bodily pain, mental health, perceptions, personal time impact, parent emotional impact and family activities). Interestingly, significant group differences were not found for the behaviour, self-esteem and family cohesion dimensions of the CHQ (Cunningham, Drotar, Palermo, McGowan, & Arendt, 2007).

Another commonly used generic HRQoL measure used to compare children with chronic illness and their healthy peers is the Pediatric Quality of Life Inventory (PedsQL™). This is a 23-item measure that yields a total HRQoL score and two summary scores based on physical and psychological health. The physical health summary score is based on scores from a physical health domain score, and the psychological health summary score is based on emotional, social and school functioning domain scores (Varni et al., 2001). Using this measure, Kunz et al. (2010), compared a sample with IBD to a healthy sample finding that participants with IBD had significantly lower total HRQoL scores compared to the healthy sample. Differences in HRQoL scores between these two groups appeared to be a result of significant differences in the psychosocial health scores, derived from significantly lower school functioning domain scores, while the social and emotional functioning domain scores were comparable to that of their healthy peers. The authors suggested that this might provide evidence that psychological adjustment is possible in young people with IBD. However, this should be interpreted with caution, as 65.3% of the youth with IBD sample had inactive disease, and it is unclear what

influence this may have had on HRQoL scores. A similar study compared participants with functional gastrointestinal disorders (chronic constipation, functional abdominal pain, irritable bowel syndrome and functional dyspepsia) and organic gastrointestinal disorders (Crohn's disease, ulcerative colitis and gastroesophageal reflux disease) with healthy controls. They found that participants with organic GI diseases had significantly lower HRQoL scores across all dimensions of the PedsQL™, with the exception of the social functioning domain scores (Varni et al., 2015). The findings that social functioning was not impaired in participants with IBD is interesting, given the existing literature that suggests a high potential for impaired social functioning in children and adolescents.

Utilising a different generic HRQoL measure, the Dutch Children's AZL/TNO Quality of Life Questionnaire (DUCATQOL), was used by Boer et al. (2005), to compare adolescent IBD patients with healthy controls. This questionnaire is a generic 25-item self-reported measure specifically for children aged 5-16 years which measures domains that capture family functioning; emotional, physical, and social functioning (Kolsteren, Koopman, Schalekamp, & Mearin, 2001). A sample of 40 adolescents with IBD was compared to 267 children from a reference database to assess the impact of IBD on HRQoL, self-esteem, and anxiety. Results indicated that boys differed significantly from the control group on the total HRQoL score, as well as three of the domains. Again, the healthy and IBD sample did not differ in the social functioning domain (Boer et al., 2005). Thus far, while the literature makes it clear that the overall HRQoL is worse in those with IBD, social functioning scores appear to be comparable to healthy peers.

Finally, Haapamäki, Roine, Sintonen, and Kolho (2011), assessed HRQoL in participants with an IBD diagnosis, using the 15D, a generic HRQoL instrument that assesses 15 dimensions

of quality of life, including breathing, mental function, speech (communication), vision, mobility, usual activities, vitality, hearing, eating, elimination, sleeping, distress, discomfort and symptoms, sexual activity and depression (Sintonen, 1994). It is worth noting that less than 10% of participants had severe disease, and the majority reported no or only minor symptoms of IBD. Nevertheless, results indicated that participants aged 12 to 19 years demonstrated lower HRQoL than their healthy peers, while those aged 7 to 11 demonstrated comparable HRQoL scores to their healthy peers. Across all participants, total HRQoL was significantly correlated with disease activity.

HRQoL and disease severity.

The research above has suggested that HRQoL is indeed negatively impacted in children and adolescents with IBD. Factors that might influence this negative impact on HRQoL have also been investigated. Specifically, it is known that HRQoL scores according to the IMPACT-III correlates well with disease activity. The IMPACT-III is an IBD specific HRQoL questionnaire, that is widely used in the paediatric IBD population. This measure (described further in the methods section of this paper) contains 35 questions covering the six domains of bowel symptoms, systemic symptoms, emotional functioning, social functioning, body image, and treatment/interventions (Otley et al., 2002). Chouliaras et al. (2017), used the IMPACT-III to assess HRQoL, and the Physicians Global Assessment (PGA), the Paediatric Crohn's Disease Activity Index (PCDAI), and the Paediatric Ulcerative Colitis Activity Index (PUCAI) to assess disease severity in IBD patients. Results indicated that disease activity was in fact correlated with total HRQoL scores, in that total HRQoL scores decreased as severity of disease worsened. These findings are further supported by other research which has also found a negative

relationship between disease activity and HRQoL (Boer et al., 2005; Engelmann et al., 2015; Gray et al., 2015; Gray, Denson, Baldassano, & Hommel, 2011; J. Haapamäki et al., 2011; Hill et al., 2010; Kunz et al., 2010; Loonen, Grootenhuis, Last, Koopman, & Derkx, 2002). This relationship is such that those with moderate to severe disease have been identified as having the lowest HRQoL scores, compared to those with mild to moderate disease (Hill et al. 2010).

HRQoL and paediatric IBD research in New Zealand.

At the time of the current investigation, only one study to date has examined the relationship between HRQoL and IBD in children and adolescents living in New Zealand. Lowe, Kenwright, Wyeth, and Blair (2012) recruited participants in the Wellington region aged 9-18 years with a diagnosis of Crohn's Disease. Researchers utilized the IMPACT-III questionnaire to measure HRQoL, and results indicated that there was no significant difference in total HRQoL scores between boys and girls. They also found a positive correlation between disease duration and quality of life, with participants who had CD longer exhibiting higher total HRQoL. Secondly, they also found a negative correlation between disease activity and quality of life, with participants with more severe disease exhibiting lower total HRQoL. As well as quantitative assessment, this study involved analyses of an open-ended question, that is included at the end of the IMPACT-III questionnaire. This question asks respondents to comment on anything they believe is important or any other comments they wish to mention. This qualitative information indicated that participants confirmed the chronic nature of CD and its treatment was distressing. Further, some children added that treatment regimens were long and tiring, and they found visual reminders of CD, such as the presence of a nasogastric tube embarrassing. Finally, participants indicated that they didn't know anyone else of their age who had IBD. These comments from the

young participants with CD are striking, as they indicate that there are negative feelings about treatment, as well as the lack of peers and subsequent social isolation. Intuitively, this may indicate that these young people found it difficult not having anyone to relate to with the same disease.

It is clear that IBD has the potential to significantly affect the lives of children and adolescents, particularly their social functioning. This becomes even more alarming given the increasing prevalence rates of IBD in New Zealand. Thus, it is imperative to understand how children and adolescents lives are impacted by the symptoms and even the treatment for this disease. For example, using HRQoL, which takes into account physical, psychological/emotional, academic, and social functioning, in addition to clinical indicators of health can help us understand this illness better as well as the lived experience of children with IBD.

While a plethora of literature exists that focuses on the HRQoL of adult patients, very little is known about the paediatric population. Consequently, it is not difficult to see the importance of this particular line of research, especially in light of the fact that only a single study has been conducted in this area. Therefore, the current study aims to contribute to the research which examines the effects IBD can have on the HRQoL in children and adolescents in New Zealand.

Hypotheses

1. It was hypothesised that the IMPACT-III measure would exhibit good to excellent internal reliability scores, as measured by Cronbach's alpha; α calculations.
2. It was hypothesised that disease severity would significantly predict social functioning, such that higher disease severity would predict lower social functioning scores.
3. It was hypothesised that disease severity would significantly predict overall HRQoL such that higher disease severity would predict lower scores of overall HRQoL.
4. It was hypothesised that disease severity would significantly predict individual HRQoL scores, such that higher disease severity would predict lower scores on the bowel, systemic, emotional and treatment/intervention subscales on the IMPACT-III.
5. It was hypothesised that duration of disease would significantly predict HRQoL such that longer disease duration would predict lower scores of HRQoL.

Methods

This project contributes to the larger Crohn's and Colitis in Children Study (CCCS), a multifaceted project that examines several different aspects of IBD in children and young adolescents. This project is being conducted through Christchurch Hospital within the University of Otago Christchurch, in Christchurch, New Zealand, with ethics approval from the Health and Disability Ethics Committee (HDEC).

The purpose of the CCCS is to define the patterns and impact of IBD in NZ children and adolescents, in order to create and develop better tools for the assessment of gut inflammation, and improving outcomes for young people with IBD. For example, the establishment of faecal biomarkers that help to predict the risk of relapse and disease complication, which would then permit customization and optimization of therapy and individualised treatment programmes. Specific research goals for the CCCS include identifying epidemiology, disease outcomes, disease patterns (e.g., presentation patterns, environmental exposure factors pre-diagnosis), genetics, and the psychosocial impact IBD can have on patients and their families.

Participants

Eligibility criteria for inclusion focused on patients who were aged 18 years or less, who resided in the South Island, and had a confirmed diagnosis of IBD (i.e., CD, UC, or IBDU). Diagnostic criteria were based upon standardised criteria, with endoscopic, histological and radiological investigations, with chart reviews performed to "flag" potential participants. Participants that met initial eligibility requirements were recruited not long after diagnosis from a large paediatric gastroenterology outpatient clinic, held at Christchurch Hospital, New Zealand, as well as from outreach clinics at hospitals throughout the South Island. Potential study

participants were approached by their paediatric gastroenterologist during their outpatient clinic appointments, who explained the study in length and provided them with a written information statement that described the study details. If they agreed to participate, written parental informed consent and child assent were obtained for children under 16 years of age and informed consent obtained directly from those over 16 years of age. As two participants did not complete consent forms, they were subsequently excluded from the study.

Procedure

Upon enrolment into the study, participants were asked to complete a research questionnaire packet while they waited in the waiting room for their clinic appointment, which included a questionnaire about IBD-related knowledge, a questionnaire about early life events, and the IMPACT-III. All other details were obtained from clinical records, with the consent of participants and their parents. Any participants that were unable to finish the questionnaires during their appointment completed the questionnaires at home and returned them in a previously-addressed and pre-paid postage envelope.

At the time of the family's appointment, the paediatric gastroenterologist undertook a baseline assessment of illness severity that included measurement of faecal inflammatory biomarkers, systemic inflammatory markers (blood), nutrition (anthropometric measurements), along with an assessment of disease activity utilising PCDAI/PUCAI and PGA measures.

HRQoL

IMPACT-III.

To evaluate IBD-specific HRQoL in children and adolescents, the IMPACT-III was given to patients during the initial recruitment process. As discussed previously, the IMPACT-III is one of the most commonly used disease-specific measures of HRQoL in the paediatric IBD

population. The current version, the IMPACT III is available in over 40 languages, as well as culturally adapted versions for English, French and Spanish (Grant & Otley, 2017).

This questionnaire is specifically designed to be used with children aged 8-18 years, and is a self-administered tool which contains 35 questions covering six domains, (bowel, body image, functional/social impairment, emotional impairment, tests/treatments and systemic impairment). Participants respond to each question on a five-point Likert scale *(e.g. 'how often have you been worrying about having a flare up (increase in symptoms) in the last two weeks? Never, Rarely, Sometimes, Often, Very Often)*. For scoring purposes, responses are numbered five through one, from left to right. Higher scores on each of the domains and in the overall HRQoL scores suggest a better quality of life (Otley, 2005).

The current version of the IMPACT measure presents with good to excellent reliability (A. Otley et al., 2006; Uggla, Lindh, Lind, & Lindkvist, 2018). For example, Otley et al. (2006) found that the IMPACT-III had excellent reliability ($\alpha = 0.92$), with the exception of the treatment/intervention subscale which was lower ($\alpha = 0.56$). The measure was also shown to differentiate between those with severe and inactive disease, with higher disease activity related to lower HRQoL scores. Uggla et al. (2018) also conducted a reliability analyses of the IMPACT-III with 194 children and adolescents who completed the IMPACT-III and a generic HRQoL measure, the Paediatric Quality of Life Inventory 4.0 Generic Core Scale (PedsQL™). Analyses showed an excellent Cronbach's alpha for the total IMPACT score ($\alpha = 0.93$). Test-retest reliability was evaluated by having 28 participants answer the questionnaires again, on average 80 days later. A paired t-test showed no significant differences between the first and second administration, and the intraclass correlation between the two tests was 0.95. They also found that the IMPACT-III demonstrated high concurrent validity, with a high correlation between the

IMPACT-III total scores and the PedsQL total scores, and satisfactory correlations between the subscales. These findings are significant, given that the PedsQL is a widely recognised and known generic HRQoL measure.

Disease Severity Measures

Paediatric Crohn's Disease Activity Index (PCDAI).

To evaluate disease severity among the participants with CD, the current investigation utilised the Paediatric Crohn's Disease Activity Index (PCDAI) which is a physician-administered multiple-item measure suitable for paediatric patients with CD aged between 0-18 years of age (Turner et al., 2007). The PCDAI can be seen as one of the most widely used measures of disease activity in CD since its development in 1991, and was created in response to the adult Crohn's Disease Activity Index that did not account for disease features that are unique to the paediatric population with CD (Loonen, Griffiths, Merkus, & Derx, 2003).

The PCDAI is an internationally accepted, multi-item outcome measure that takes into account disease features that are unique to children with CD. This measure consists of a physical examination (i.e., weight, height, abdominal examination, perirectal disease, and extra-intestinal manifestations of illness), three common laboratory tests (i.e., haematocrit, erythrocyte sedimentation rate, and albumin) and assessment of subjective symptoms (i.e., patient reported abdominal pain, number of liquid stools, general well-being (Loonen et al., 2003). Each index item is assigned a score from 0-10, with zero representing normal, five representing a mild abnormality, and ten representing a severe abnormality. After rating each category, a patient is rated overall from 0-100 (Hyams et al., 1991). An overall score greater than 30 signifies moderate to severe disease whilst a score between 0 and 10 signifying inactive disease.

The reliability and validity of the PCDAI have been evaluated in a few studies.

Specifically, Hyams et al. (1991) tested the validity of the measure 133 paediatric patients with CD, and found that the measure possessed good concurrent validity as evidenced by a significant correlation between the PCDAI and physicians global assessment (PGA) ($r = 0.80$, $p = 0.001$). Similarly, they reported excellent interobserver agreement for total PCDAI scores and PGA ($r = 0.86$, $p = 0.001$). In a separate study, Hyams et al. (2005), further evaluated the PCDAI in 181 patients in a multicentre study from the United States and Canada. Results indicated that PCDAI scores were correlated with PGA scores, and pairwise mean comparisons indicated the measure was able to discriminate between disease severity (i.e., mild vs. moderate, mild vs. severe, moderate vs severe).

Paediatric Ulcerative Colitis Activity Index (PUCAI).

In the current study, the Paediatric Ulcerative Colitis Activity Index (PUCAI) was utilised to assess disease severity in children with UC. The PUCAI is a physician-administered multiple-item measure suitable for paediatric patients with UC aged between 0-18 years of age.

In terms of the metrics of the measure, a score of less than 10 indicates no or inactive disease, 10-34 indicates mild disease, 35-64 indicates moderate disease, and a score equal to or greater than 65 indicates severe disease (Turner et al., 2009). In order to determine disease activity in adults, a sigmoidoscopy (i.e., use of a scope to look inside the rectum and lower colon) is performed, however, this is less tolerated by paediatric patients. Instead, the PUCAI measures patient reported abdominal pain, rectal bleeding, stool consistency, number of stools, nocturnal stools, and amount of activity that is limited (Turner et al., 2007).

Turner et al. (2009) evaluated the reliability and validity of the PUCAI in 215 children with UC. Results indicated that the PUCAI was highly correlated with the PGA ($r = 0.90$, $P <$

0.001), and did not differ significantly based on location of disease ($r = 0.88$ and 0.91; $P < 0.05$). Additionally, median PUCAI scores were higher in patients whose therapy had escalated compared to those whose therapy decreased or remained unchanged, and PUCAI scores were also predictive of the need for escalating therapy. In terms of reliability, the PUCAI evidenced excellent test-retest reliability (ICC = 0.89, $P < 0.001$).

Paris Classification for Crohn's Disease and Ulcerative Colitis

The Montreal classification was developed to classify IBD patients according to phenotypic characteristics, including age, disease location, and disease behaviour (Silverberg et al., 2005). However, paediatric IBD has unique phenotypic characteristics including a greater tendency for disease extension, changes in disease location and behaviour over time which are not adequately considered with the Montreal classification. In response to this, a modification to this classification was created, which became known as the Paris Classification, which addresses those weaknesses, and takes into account the phenotypic characteristics unique to paediatric IBD (Levine et al., 2011).

The Paris modifications were created predominately in partnership with the 2nd International Symposium on Paediatric Inflammatory Bowel Disease, held in 2009. Paediatric IBD studies were identified using a uniform search strategy, with a focus on those studies which analysed phenotypes by age. Using this literature, the effect of age on endoscopic and microscopic involvement, disease phenotype and behaviour were evaluated. This review allowed for the identification of areas that required reconsideration, and assisted focus groups in preparing a consensus document with proposals for modification to the Montreal Classification. The modifications were made whilst still adhering to the framework of the Montreal Classification, which allowed for the classification to be used in both paediatric and adult

patients (Levine et al., 2011).

The Paris Classification of paediatric IBD classifies CD patients according to age, location, behaviour and growth. A paediatric patient is classified as either less than 10 or 10-17 years of age (Levine et al., 2011). This distinction was made to separate very young children and older children, as the Montreal Classification classed paediatric patients as either less than 16 or between 17- 40 years of age. This change was further supported by a significant amount of data suggesting that young age at onset of CD is associated with differing disease phenotypic characteristics than those above the age of 8-10 years (Hyams, 2014).

It is of importance to define disease location and disease behaviour in CD, as it directly influences the choice of therapy (Hyams, 2014). Disease location is typically classed as one of five categories based on the location of disease in the gastrointestinal tract, however the Paris classification included the addition of two categories, to distinguish between jejunal disease and upper gastrointestinal disease (oesophagus, stomach and duodenum), which is commonly examined as part of initial evaluation by paediatric gastroenterologists (Hyams, 2014).

Classification of disease behaviour remains the same between the Montreal and Paris classifications, with disease being either non-stricturing non penetrating (inflammatory), penetrating or stricturing (Levine et al., 2011). However, an additional category was added in response to a later study that showed that penetrating and stricturing CD can be demonstrated independently or they can coexist with each other. The Paris classification also added the presence of growth delay, as it was widely known that growth delay is common in paediatric CD and is an important consideration in treatment decisions. For example, corticosteroids are known to inhibit growth, whereas EEN and biologics have been shown to improve or promote growth (Hyams, 2014).

The Paris classification classifies patients with UC based on the extent and severity of disease. Disease severity was previously considered either in remission, mild, moderate, or severe, however the Paris modifications recognised data suggesting PUCAI (UC disease severity score) scores were important clinical indicators of response to treatment and need for surgeries, thus changed disease severity to either S0 for no presence of severe disease, and S1 indicating severe disease at any time in the patient history (PUCAI $\geq$ 65). Disease extent is based on the location of disease within the colon, and patients are assigned one of 4 categories (Levine et al., 2011).

Physician's Global Assessment (PGA)

The Physician's Global Assessment is a widely used and accepted measure of disease severity in IBD that is based on the clinical judgement of a specialist who completes a clinical evaluation. Specifically, after an evaluation a physician classifies IBD patients into one of four groups: 1) inactive, 2) mild, 3) moderate or 4) severe disease activity. Whilst the PCDAI incorporates clinical symptoms, physical examination and laboratory parameters, the PGA demonstrated strong correlations with other measures of disease severity, including the PCDAI (J. Hyams et al., 1991) and PCDAI (Turner et al., 2009).

As the PGA relies on the individual clinical judgement of the physician, the current study had the same physician completing the PGA's for all the study participants.

Results

Analyses

Preliminary transformations and analyses.

The current study included analyses of data collected as part of the Crohn's and Colitis in Children study, as described in detail on page 35-36. All preliminary analyses, transformations, and primary analyses were conducted using IBM SPSS version 25 (Armonk, NY: IBM Corp.). The CCCS primary research fellow provided data in two separate Microsoft Excel spreadsheets, with one containing participant information such as demographics, diagnosis, date of birth etc., and the other containing each participant's scores from the IMPACT-III questionnaire. These spreadsheets were imported and merged into a single master database in SPSS. The database was "cleaned" to remove any spelling or input inconsistencies, with new variables created that were deemed essential to the current investigation. For example, the age of each participant at the time of first questionnaire completion was calculated, using the participant's date of birth, and date of questionnaire completion. Additionally, participant ID codes were re-formatted into numerical form, and data was reformatted so each line number contained all the information for each individual participant.

To determine disease duration, the number of months between each participant's diagnosis date and the first questionnaire assessment date were calculated. Similarly, the age of each participant at the first assessment time point, the amount of months between birthdate and that first assessment date were calculated. From this, the month total was converted to a single or double-digit age number (e.g., 12.28). Disease severity scores were based on the Physicians Global Assessment (PGA) and the Paediatric Crohn's Disease Activity Index (PCDAI) / Paediatric Ulcerative Colitis Activity Index (PUCAI). Each subscale of the IMPACT-III was

labelled as either Bowel, Systemic, Emotional, Social, Body Image, and Treatment/Intervention. Reliability checks were conducted during this process to ensure no mistakes had been made with variable editing and data transformation. This was done by randomly selecting 25% of the participant ID numbers, and checking the original data documents to ensure all data were entered correctly. Any missing data points were identified, at which point the CCCS research fellow was contacted to obtain missing data where possible.

As the PCDAI and PUCAI measures use the same metric for disease severity and use identical cut-off scores (i.e., remission, mild, moderate and severe; (Turner et al., 2009; Turner et al., 2007), these measures were not analysed separately. Demographic variables (e.g., age, gender, and ethnicity, location of residence) were examined for descriptive purposes (Table 1).

Table 1:

Demographic information for the study sample

	n	m	%	SD
Age at Time 1	91	13.37		2.207
Age at Diagnosis	91	10.75		
Gender				
Male	56		61.5	
Female	35		38.5	
Total	91			
Ethnicity				
Pakeha/NZ European	89		97.8	
European	1		1.1	
Eurasian	1		1.1	
Diagnosis				
Crohn's Disease	79		86.8	
Ulcerative Colitis	9		9.9	
IBD-Unclassified	3		3.3	
Location				
Christchurch	53		58.3	
Canterbury	11		12.1	
South Island	27		29.7	

Pearson correlations and T-tests were conducted to assess the degree to which participant demographic variables were associated with the primary variables of interest (e.g., HRQoL, disease severity, disease location, disease duration). Results indicated that there were no significant relationships between demographic variables and primary variables of interest. Consequently, no demographic variables were controlled for in subsequent analyses.

To determine if significant differences existed between males and females, and those with active and non-active disease on key variables of interest, an independent-samples t-test was carried out (Table 2). Results indicated no significant group differences on total IMPACT-III scores for males or females, and no significant differences in scores of disease severity. Consequently, no demographic variables were controlled for in subsequent primary analyses.

Similarly, results indicated no significant group differences on total IMPACT scores for those with active and inactive disease, and no significant differences on any on the IMPACT-III subscales.

Table 2

Differences between males and females measures of QoL and disease severity

	Male	Female		
Variable	M (SD)	M (SD)	t	p
PGA	0.83 (0.9)	0.68 (0.8)	0.73	.32
PCDAI/PUCAI	13.44 (13.7)	9.54 (12.2)	1.2	.09
Total IMPACT	22.16 (3.6)	21.27 (3.5)	1.12	1.1
Bowel Symptoms	27.15 (4.9)	25.39 (5.8)	1.4	.22
Systemic Symptoms	10.59 (3.1)	9.52 (2.8)	1.6	.68
Emotional Functioning	26.04 (6.3)	24.94 (5.9)	0.8	.80
Social Functioning	47.65 (8.1)	47.0 (7.2)	0.37	.54
Body Image	10.57 (2.2)	9.94 (2.1)	1.3	.38
Treatment/Intervention	11.30 (2.9)	10.85 (2.6)	0.72	.30

Table 3

Differences between active and non-active disease groups

	Active Disease	Non-Active Disease		
Variable	M (SD)	M (SD)	t	p
Bowel Symptoms	27.74 (5.80)	25.24 (4.96)	2.10	.72
Systemic Symptoms	11.08 (2.95)	9.62 (3.08)	2.17	.55
Emotional Symptoms	27.31 (5.68)	24.31 (6.4)	2.21	.43
Social Symptoms	49.72 (7.10)	45.62 (8.25)	2.39	.23
Body Image	10.85 (2.57)	10.05 (2.57)	1.63	.10
Treatment/Intervention	11.16 (2.83)	11.05 (1.79)	.172	.88
Total	137.55 (22.37)	125.88 (20.69)	1.12	.91

The internal consistency of the IMPACT-III was examined by calculating Cronbach's alphas for the total scores and each individual subscale of the measure (Table 4).

Table 4:

Means, standard deviations and reliability coefficients of the IMPACT-III and subscales

Subscales	N (items)	M (SD)	Cronbach's Alpha
Total	35	130.94 (21.6)	.93
Bowel	7	26.48 (5.36)	.76
Systemic	3	10.18 (3.07)	.85
Emotional	7	25.52 (6.18)	.84
Social	12	47.4 (7.79)	.83
Body Image	3	10.33 (2.2)	.58
Treatment/Intervention	3	11.13 (2.82)	.62

Descriptive Statistics.

Demographic variables were examined for descriptive purposes (Table 1). The average age of the participants was 13.37 years of age and 61.5% were male. The majority of the participants described their ethnicity as Pakeha/New Zealand European, and lived in Christchurch.

Descriptive statistical analyses indicated that the average age at diagnosis was 10.75 years, with a diagnosis of CD being most common. The most common disease location was disease involved the terminal ileum and colon (L3), and 90% of participants demonstrated inflammatory (B1) disease behaviour (Table 5). Means and standard deviations for the IMPACT-III questionnaire were calculated (Table 4). The average score across all participants was 130.94

Table 5:

Descriptive statistics for the study sample

	n	%
Disease Activity		
Active	39	48.1
Inactive	42	51.9
Disease Behaviour		
B1	63	90
B1p	3	4.3
B2	1	1.4
B3	1	1.4
B3p	1	1.4
p	1	1.4

Table 6

Disease location statistics

	n	%
Disease location		
L1	12	14
L1 + Upper Disease	2	2
L1 + p	3	4
L2	4	5
L2 + Upper Disease	11	13
L3	14	16
L3 + Upper Disease	25	29
L4	1	1
E1	1	1
E4	10	12
p	2	2

Primary analyses.

To examine the relationship between disease severity and social functioning, 2 regression analyses were conducted. Results indicated that disease severity measured by the PGA did indeed predict social functioning $F(1,79) = 7.558$, $p < .05$, such that participants with more greater disease severity, as measured by the PGA, exhibited poorer social functioning. Similarly, results from additional regression analysis indicated that disease severity, as measured by the PCDAI/PUCAI, also predicted social functioning $F(1,79) = 7.558$, $p < .05$. That is, participants

with more severe disease, as measured by the PCDAI/PUCAI, exhibited poorer social functioning.

To test the hypothesis that the IMPACT-III would exhibit good to excellent internal reliability scores (Table 4), Cronbach's α were calculated for the IMPACT-III and each of the individual subscales. Results indicated excellent internal consistency for the total score (α = .93) and adequate to excellent scores for the subscales (e.g., α = .58 to α = .85).

To test the hypothesis that illness severity would predict child HRQoL, several regression analyses were conducted. Specifically, to examine the relationship between illness severity measured by the PGA and overall HRQoL, participant PGA was entered as the independent variable and total scores from the IMPACT-III were entered as the dependant variable. Results indicated that PGA scores significantly predicted total HRQoL scores, $F(1,78) = 8.42$, $p < 0.01$, suggesting that participants with greater disease severity exhibited poorer overall HRQoL (Table 7).

To examine the relationship between illness severity measured by the PCDAI/PUCAI and overall HRQoL, participant PCDAI/PUCAI was entered as the independent variable and total scores from the IMPACT-III was entered as the dependant variable. Results indicated that PCDAI/PUCAI scores significantly predicted total HRQoL scores, $F(1,75) = 6.896$, $p < 0.01$, indicating that participants with greater disease severity exhibited poorer overall HRQoL (Table 7).

Secondary Analyses.

To test the hypothesis that disease severity would predict HRQoL scores on the individual IMPACT-III subscales, separate analyses were run with disease severity as measured by the PCDAI/PUCAI entered as the independent variable and each individual subscale of the

IMPACT-III measure entered as the dependant variable. Results indicated that disease severity significantly predicted scores on the bowel subscale, $F(1,76) = 7.972$, $p > .05$, as well as the systemic subscale $F(1, 79) = 5.870$, $p < .05$ and emotional subscale $F(1,79) = 6.568$, $p < .05$ Similarly, the PCDAI/PUCAI did not significantly predict HRQoL scores on the body image subscale $F(1,78) = .925$, $p > .05$, or the treatment intervention subscale $F(1,75) = .074$, $p < .05$ (Table 7).

Similarly, analyses were run with disease severity measured by the PGA entered as the independent variable and each individual subscale of the IMPACT-III measure as the dependant variable. Results indicated that disease severity significantly predicted scores on the bowel subscale $F(1,79) = 6.550$, $p < .05$, systemic subscale $F(1,79) = 6.550$, $p < .01$, and emotional subscale $F(1,79) = 6.568$, $p < .05$. This tells us that those with more severe disease according to the PGA have poorer HRQoL ratings on the bowel, systemic, emotional and social subscales of the IMPACT-III. Disease severity according to the PGA did not significantly predict HRQoL scores on the body image subscale $F(1,79) = 1.935$, $p > .05$, or the treatment/intervention subscale $F(1,78) = .750$, $p > .05$ (Table 8).

To test the hypothesis that disease duration would significantly predict total HRQoL, a regression analysis was conducted. Disease duration was entered as the independent variable, and total HRQoL scores from the IMPACT-III were entered as the dependant variable. Results indicated that disease duration did not significantly predict total HRQoL, $F(1,84) = 8.78$, $p > .05$.

Table 7

Regression Analyses between IMPACT-III questionnaire and the Disease Severity Measures

	R^2	β	B	SE B
PCDAI/PUCAI T1				
Total IMPACT T1	.084**	-.290	-.482	.184
Bowel Symptoms 1	.095**	-.308	-.129	.046
Systemic Symptoms 1	.072*	-.268	-.061	.025
Emotional Symptoms 1	.053*	-.230	-.108	.052
Social Functioning 1	.081*	-.285	-.170	.065
Body Image 1	.012	-.110	-.018	-.110
Treatment/Intervention 1	.001	-.031	-.007	.025

*p <.05, **p < .01

Table 8

Regression Analyses between IMPACT-III questionnaire and the Disease Severity Measures

	R^2	β	B	SE B
PGA T1				
Total IMPACT T1	.097**	-.312	-7.848	2.704
Bowel Symptoms 1	.077**	-.277	-1.726	.674
Systemic Symptoms 1	.268*	-.268	-.939	.380
Emotional Symptoms 1	.077*	-.277	-1.959	.764
Social Functioning 1	.087*	-.295	-2.667	.970
Body Image 1	.024	-.155	-.391	.281
Treatment/Intervention 1	.010	-.098	-.315	.363

*p <.05, **p < .01

Discussion

The primary aim of the current study was to examine the relationship between disease severity and HRQoL in children and adolescents with IBD. HRQoL scores measured by the IMPACT-III were examined to ascertain if disease severity was a significant predictor of HRQoL. A specific focus of the study was to understand what, if any, impact that disease severity has on social functioning.

After a thorough search of the available literature, it was hypothesised that the IMPACT-III measure would exhibit good to excellent internal reliability scores, as measured by Cronbach's α scores. This was an important first step, as the reliability of this measure would be crucial for establishing a better understanding of the relationship between HRQoL and IBD-related variables. Secondly, it was hypothesised that disease severity would significantly predict HRQoL scores, with higher disease severity predicting lower scores of HRQoL. Thirdly, that disease severity would be a significant predictor of social functioning. Finally, it was predicted that the duration of disease would significantly predict HRQoL, such that longer disease duration would predict lower scores of HRQoL. The present study revealed some important and interesting findings. As hypothesised, the IMPACT-III demonstrated excellent internal reliability. Two measures of disease severity were significant predictors of HRQoL, while disease duration was not a significant predictor of HRQoL. Of note, the analysis showed that social functioning was a significant predictor of HRQoL, thus supporting the hypothesis in the current investigation.

Internal Reliability of the IMPACT-III

As mentioned earlier in this paper, the IMPACT-III's reliability has been assessed in a

handful of studies, all of which demonstrate good to excellent reliability scores overall. It is still important to assess the reliability of the instrument in this current study, given that reliability is dependent on the particular sample being tested (Streiner, 2003), therefore reliability in the current sample cannot be guaranteed. Determining reliability for the current sample will allow the researcher to confirm the psychometric rigour of the measure that is being used to derive conclusions. Confirming the reliability of this measure is also particularly important, given that it is a widely used measure for the assessment of HRQoL in paediatric patients with IBD.

Reliability analyses confirmed the hypothesis that the IMPACT-III would evidence good to excellent reliability. Specifically, the total scores had an excellent Cronbach α, indicating that the measure shows excellent internal consistency. Each individual subscale of the IMPACT-III showed acceptable to good reliability, with the exception of the treatment/intervention and body image subscales Similar findings have been reported in other validation studies, with low reliability for these two subscales (Loonen, Grootenhuis, Last, Haan, et al., 2002; Uggla et al., 2018). It is known that Cronbach's α is strongly affected by the length of a scale (Streiner, 2003), thus this finding is not unexpected, given the treatment/intervention and body image subscale each contain three items. Further investigation into this matter would contribute to further validation of the IMPACT-III.

HRQoL and Disease Severity

The current study was able to confirm that disease severity was a significant predictor of HRQoL, which is similar to research by Gray et al. (2015). While there is limited research determining if disease severity is a predictor of HRQoL, research has demonstrated significant correlations between disease severity and HRQoL (Gray et al., 2011; Hill et al., 2010; Lowe et

al., 2012; Otley et al., 2006). These findings are of particular importance as it demonstrates that characteristics of disease such as disease severity, are a significant factor involved in HRQoL with IBD.

While the primary focus of the current study was to understand the relationship between disease severity and social functioning, further analyses were conducted to clarify if disease severity was related to the other subscales on the IMPACT-III. The current study demonstrated that disease severity was a significant predictor of the bowel, systemic and emotional subscales of the IMPACT-III, but not the treatment/intervention and body image subscales. While few studies have examined predictors of disease severity, Hill et al. (2010) found that disease severity was significantly correlated with each subscale of the IMPACT-III. This contrasts the current findings, however, due to differences in statistical analyses, it is unclear if this relationship would remain to the extent that the treatment/intervention and body image would remain significant predictors of disease severity in regression analyses.

Social Functioning and Disease Severity.

A critical finding of the current study was that all measures of disease severity (i.e., PGA & PCDAI/PUCAI), were significant predictors of social functioning. This finding is similar to that of previous research, which found that disease severity was significantly correlated to social functioning (Chouliaras et al., 2017; Cunningham et al., 2007; Gallo et al., 2014; Hill et al., 2010). However, a study by Kunz et al. (2010), contradicts the current findings by finding that youth with active or inactive disease did not differ significantly on HRQoL domains of the PedsQL, which included social functioning. Three of the four studies that supported the current findings used the IMPACT-III, and the fourth used the CHQ. It is noted the study by Kunz et al. (2010) used the PedsQL to measure HRQoL. It is possible that differences between the HRQoL

measures led to a difference in findings. However the PedsQL has been shown to correlate significantly with the IMPACT-III (Abdovic et al., 2013; Uggla et al., 2018), so the cause of this difference is unclear. It should also be noted that the research supporting the current findings used small numbers of participants or had participants with primarily inactive disease, which is not uncommon for most paediatric IBD research undertaken. This should be kept in mind when considering the results.

The findings that disease severity significantly predicts overall HRQoL highlight the importance of initiating remission in these patients as quickly and safely as possible, to ensure minimisation of detrimental impacts on HRQoL and social functioning. This is particularly salient given childhood and adolescence are known to be critical stages of social and emotional development. Further investigation into the effects of disease and HRQoL could be beneficial to attempt to understand what makes a child or adolescent more likely to function well, despite having a chronic illness, thus helping researchers and health professionals to understand what protective factors and coping mechanisms should be promoted in children.

HRQoL and Disease Duration

The hypothesis that disease duration was a significant predictor of paediatric HRQoL was not supported in the current investigation. Literature on this particular topic appears to be limited at this stage, however some studies have reported significant correlations between disease duration and HRQoL (Chouliaras et al., 2017; Otley et al., 2006), and others have found no significant relationships (Haapamäki et al., 2010; Hill et al., 2010). While specific reasons for these mixed findings are unclear, it might be expected that disease duration would have an impact on HRQoL, given the nature of IBD. In particular, management of disease typically

improves over time (Otley et al., 2006), which would be expected to have a positive influence on the HRQoL of individuals. While disease management has been shown improve over time in some cases, which might account for the research finding improved HRQoL over time, the current findings might be reflective of those whose disease was not well managed, or those who had recently experienced a flare-up in disease activity. Considering the limited research available on this topic, further research is warranted to better understand factors that might be associated with or influencing the likelihood of disease duration having a positive effect on HRQoL scores.

Limitations

There are some limitations of the current study that must be considered. Of note, the lack of diversity of the participants, with the majority of participants identifying themselves as NZ/European. This is not representative of New Zealand's IBD population as it does not include a range of ethnicities such as Māori or Pacific Islanders. A study by Lopez et al. (2017) found that of their 212 paediatric IBD patients identified in New Zealand, 86.8% were European, 9.9% were Asian, 4.2% were Māori and 1.4% were Pacific Islander and Middle Eastern. As a result, the generalisability of the current findings must be interpreted with caution when considering other racial or ethnic groups.

A further limitation of this study is the data collection. Unfortunately, due to the expected nature of research studies, there was a large amount of missing or incomplete data which reduced the sample size. Whilst the cross-sectional design of the study allowed for a total of eight separate opportunities to complete the questionnaire, only a small amount of participants completed all eight. As a result of this, given the restrictions of the current study, only data taken at one time-point was included. Future research utilising a longitudinal design would further develop the findings from the current investigation.

Due to the nature of the study and the disease-specific IMPACT-III questionnaire, there was no opportunity to compare HRQoL scores to health norms. Although previous research has examined this particular question in other geographic locations, understanding the potentially different experiences of children and adolescents with IBD in New Zealand can be seen as an important next step in this line of research. For example, this data could ultimately help establish clinical cut-offs, to help health professionals understand the effects of disease upon HRQoL of the individuals with IBD.

A final limitation of this study was the lack of ability to compare those with CD to those with UC. Unfortunately, only a small amount of participants were diagnosed with UC, with the majority of the sample having CD. This did not allow sufficient sample size to complete analyses comparing these two groups, which would have been of interest. Future research could address the differences between these two types of IBD disease and their severity and HRQoL.

Implications and Future Directions

The finding that the IMPACT-III demonstrated good to excellent reliability in the current sample is positive, as it supports the understanding that the IMPACT-III is a reliable measure, thus promoting its use in future studies. This is particularly important, given that the use of the IMPACT-III is widespread in paediatric IBD populations (Grant & Otley, 2017).

The finding that disease severity is a significant predictor of HRQoL is significant and is generally consistent with previous research. and has significant research and clinical implications. This study supports the idea that poor management of disease can have a detrimental impact on HRQoL, and it is crucial that effective treatment of the disease from initial diagnosis occurs for children and adolescents if we are to avoid issues with growth and development that were described earlier.

This also raises questions about what is the best treatment method for this population, given they are at risk of numerous negative outcomes. While the traditional 'step up' approach is applied in most cases, this may not be appropriate or beneficial for all individuals, particularly those whose HRQoL may already be poor. The 'top-down' method of turning to more potent therapies such as biologics early on may, in some cases, be the most appropriate for children and young people with IBD, particularly as this method has the benefits of achieving and maintaining remission, avoiding growth deficiencies in paediatric IBD, avoidance of poor outcomes, and induction of mucosal healing (Hirschmann & Neurath, 2017). However, this needs to be balanced with safety concerns regarding the potentially serious side effects, although rare, which can occur. We-currently lack the ability to accurately identify those patients who are a 'high risk' for severe disease and poor outcomes who would benefit from the more expensive biologic therapies early on in their treatment. This requires further research in order to make the current biologics more accessible as well as access to new biologics as they are developed.

As noted earlier, in order to have access to the latest line of treatment, patients are expected to trial and fail at a number of other medications which potentially exposes them to a raft of risks and side effects which are concerning in their own right. The development of clinical guidelines based on a 'top-down' approach may be of benefit for this patient group, in order to avoid over-treating with multiple medications and exposure to long term side effects.

These findings highlight the need to incorporate the assessment of HRQoL within treatment and management programmes for IBD. While the design of the current study did not allow for comparison of HRQoL in those with IBD to a healthy comparison group, previous research has indicated that those with IBD do have poorer HRQoL than those who are healthy (Boer, Grootenhuis, Derkx, & Last, 2005; Cunningham, Drotar, Palermo, McGowan, & Arendt,

2007; Haapamäki, Roine, Sintonen, & Kolho, 2011; Kunz, Hommel, & Greenley, 2010).

The current study, combined with previous research clearly demonstrates that HRQoL is a critical aspect that should be considered in those patients with IBD. Ideally, data such as that derived from the current study, would lead to changes in the management of this at-risk group, to form integrated holistic care pathways that follow them throughout their IBD journey, and include the participation of carers and families. This integrated care would not solely rely on care from physicians and specialists, but include those who are trained to address the needs of a developing child or adolescent, thus providing a truly multi-disciplinary team approach.

Incorporation of a measure, such as the IMPACT-III into routine clinic assessments could provide an early indication or baseline of how the child is functioning and coping within their daily lives, and could provide a mechanism for identifying those children who are struggling, and might need extra support. For example, play therapists for younger children to help them better understand their disease through play, or child psychologists to provide early interventions to help those at risk for mental health issues, or to teach children and adolescents coping mechanisms to better live with their chronic disease. In particular, those who have been identified as having poor social functioning could be further assessed to ascertain where changes and support can be provided to mitigate any issues. Unfortunately, given the current climate of New Zealand's mental health system, it is often difficult to access services in a timely manner, particularly if the threshold for specialist services are not met. This becomes particularly concerning for young people with a chronic disease, who are at risk for poor developmental outcomes.

On this note, HRQoL could be considered when making decisions about treatment methods. For example, considering which treatments have the highest risk or side effects may be

avoided in children, particularly those children who have been identified as having poorer HRQoL. Regular assessment of HRQoL has the potential to provide a self-administered, subjective assessment of how an individual is coping with the psychosocial effects of their disease, not just the physical impacts which are currently the focus of medical treatment.

One method for addressing poor social functioning in these young IBD patients is through peer support groups. One example of this is the Chronic Illness Peer Support programme (ChIPS), which aims to improve adjustment to living with a chronic illness, increase a sense of control over health status, develop personal abilities and become more active in their local community. The programme comprised of eight discussion sessions with up to eight young people per group, and teaches participants to learn new coping techniques, learn how to influence social environments, understand the cause of personal stressors, enlarge perspectives on what is seen as normal and alternative perspectives, understand the cause of personal stressors, reduce sense of isolation, enhance identify through group cohesion, and promote extending of help to others (Olsson, Boyce, Toumbourou, & Sawyer, 2016).

In New Zealand, Camp Purple Live is a camp designed specifically for children and adolescents with IBD, which gives children a chance to attend a camp, and participate in typical camp activities that they may not otherwise be able to engage in due to their illness. McCombie, Gearry, Lopez, Lonnfors, and Day (2017) conducted a study obtaining feedback from campers who attended the camp in 2015. They found that the majority of respondents agreed that the camp improved confidence in dealing with their IBD (86.1%), improved their overall QoL (75%), and all respondents would recommend the camp to others with IBD.

Conclusion

As demonstrated, the impact of chronic diseases such as IBD on children and young people is not widely researched, however, a body of research is growing and provides insight into the impact a chronic illness have on the overall functioning of young people. The diagnosis of such a chronic disease at a young age is overwhelming and has a significant impact on overall quality of life, as well as impacting on the wider family. In young people, parents/carers play a vital role in ensuring the treatment programme is adhered to, and the perceptions of the parents/carers may provide their view on how the child is coping which may not necessarily reflect the true experience of the child. Tools and measures that help to capture the lived experience of the child are vital to ensure the overall success of the treatment programme for this disease for which there is currently no cure.

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